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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/675,650	09/29/2000	Ursula Busse	1619.0080001/SRL/TBB	1706
26111	7590	02/10/2004	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			YU, MISOOK	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/675,650

Applicant(s)

BUSSE ET AL.

Examiner

MISOOK YU, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 9-12 and 24-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 and 9 is/are allowed.
- 6) ☒ Claim(s) 1-5, 10-12 and 24-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/12/04</u> . | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet.</u> |

Continuation of Attachment(s) 6). Other: page 2 of Amendment filed on 7/11/2002.

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The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/12/2003 has been entered.

The listing of claims filed on 11/12/2003 indicates claims 7, 8, 13-23 are withdrawn from consideration but still pending. However, the remark section beginning at page 11 of the amendment states that claims 1-6, 9-12, and 24-34 are pending.

The prosecution history indicates that applicant cancelled claims 7, 8, 13-23 in the amendment filed on 7/11/2002. Note the attached page 2 of the amendment filed on 7/11/2002. Based on the prosecution history, the Office treats that claims 1-6, -6, 9-12, and 24-34 are currently pending and requests applicant to correct the status of claims in the listing of the claims in the next response.

Claim 3 is amended, claims 28-34 are new. Claims 1-6, 9-12, and 24-34 are pending, and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 3 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn because applicant amended the claim.

The Following are New Grounds of Rejection

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 25 line 27. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informalities: the specification does not identify SEQ ID NOs for each of the peptide sequences in Fig. 5. Amending the specification by listing the corresponding SEQ ID NOs listed in sequence listing at page 28 at Figure 5 legend would obviate this rejection.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 3, 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, and 27 recite "under high stringency conditions" but it is not clear what the metes and bounds are. The specification at page 13 says that hybridizing conditions are known in the art but does not define "under high stringency conditions". Since what will hybridizes depends on hybridization conditions, the claims are indefinite

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as to the property boundary by the recited limitation. This rejection affects all dependent claims. All dependent claims are also rejected.

Claim 25 recites the limitation "the open reading frame" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 26 recites "is" in line 2 but it is not clear what the metes and bounds are for the limitation. This rejection is made because the limitation could be interpreted as "comprising", "consisting of", or consisting essentially of" since its base claim 6 is drawn to a primer consisting of 10 to 50 consecutive nucleotides of nucleotide 27 to 254 of SEQ ID NO:1. Instant SEQ ID NO:4 is 20 nucleotides long so the limitation "is" could be interpreted as primer consisting of SEQ ID NO:4 or consisting essentially of and/or comprising SEQ ID NO:4 up to 50 nucleotides by adding up to 30 more nucleotides to instant SEQ ID NO:4.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 10-12, and 24, 25, 27-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has several aspects.

The claims are drawn to genus of isolated nucleic acid or a recombinant nucleic acid molecules encoding something (one of said something is SEQ ID NO:3), and to genus of cell, or non-human organism containing said recombinant nucleic molecules, genus of isolated nucleic acid comprising 27 to 254 nucleotide of SEQ ID NO:1, fully complementary to isolated nucleic acid comprising 27 to 254 nucleotide of SEQ ID NO:1, or hybridizes to 27 to 254 nucleotide of SEQ ID NO:1, genus of molecules comprises SEQ ID NO:1 (claim 4), encodes instant SEQ ID NO:3 (claim 5), .

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

First, in case of claims 1, 2, 10-12, 25, the Office could not envision how the claimed structure(s) looks like or what the function of the claimed nucleic acid molecule(s) is based on the limitation of claim 1 i.e. "a differentially expressed prostate cancer antigen 3 (PCA3) mRNA containing an additional sequence between exon 3 and exon 4a, thereby giving rise to a PCA3 mRNA, having a sequence which is longer than that set forth in SEQ ID NO:2" or based on the limitation of claims 2 and 24 "additional sequence interrupts the open reading frame of a PCA3 protein, thereby yielding a truncated PCA3 protein". PCA3 appears to be a proper noun like Bob Smith and its alias appears to be DD3. See the explanation below with Bussenmakers et al (Cancer

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Res. 1999 Dec 1;59(23):5975-9, a copy provided in the Office action mailed on 10/16/2002). The specification does not define "PCA3". Instant claims 1, 2, 10-12, 25 say that a nucleic acid sequence is inserted into a second nucleic acid sequence, resulting in third nucleic acid sequence which is longer than SEQ ID NO:2. There is not even identification of any particular structure or function in the claims.

Second, claims 1, 2, 5, 10-12, 25, 27-34 appear to claim various nucleic acid encoding a protein with undefined amino acid sequence except claim 5. The only protein sequence disclosed in the specification is SEQ ID NO:3. However, the specification at Fig. 4 discloses that instant SEQ ID NO:3 is a putative protein, its presence not yet determined experimentally. Bussenmakers et al (Cancer Res. 1999 Dec 1;59(23):5975-9) teach a PCA protein recited in instant claim 25 might be a false protein, not actually produced but hypothetical protein based on nucleotide examination. One in skill in the art would have questions whether instant SEQ ID NO: 3 is a real protein without experimental data based on Bussenmakers et al "DD3 may function as a noncoding RNA" (note page 5977). Further, claims 27 and 31 recite "complementary" sequence and the dependent claims 28 and 32 says the complementary sequences are used to make recombinant nucleic acid with a promoter such initiation of transcription occurs. Unlike prokaryotes, the human complementary DNA (antisense) usually does not encode any protein except rare occasions. The instant specification does not teach any of the complementary DNA sequences encode anything. Other problems in the claims are hybridizing nucleic molecules. The specification does not describe what kind is activity is associated with the genus of nucleic acid molecules being claimed.

Third, all the claims have open language, "comprises" in claims 3 and 4, and "having" in claims 1, 27, and 31. The specification at Figures 3 teaches that instant SEQ ID NO:1 is not an entire open reading frame but a PCR-amplified partial sequence from between two exons of a known gene, DD3 or PCA3. The specification does not teach what the entire open reading frame that includes 27 to 254 nucleotide of SEQ ID NO:1.

Any dependent claims drawn to cell or non-human organism containing the rejected nucleic acid molecules fails to provide adequate written description because they contains the rejected nucleic acid molecules.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleotide, given that the specification has only described SEQ ID NO: 1. Therefore, only SEQ ID NO:1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is separable from its enablement provision (see page 1115).

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A definition by function alone "does not suffice, to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is."

Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406.

Allowable Subject Matter

The indicated allowability of claims 1, 2, 4, 5, and 24, 25, 27 is withdrawn in view of the newly discovered reference(s) to Bussemakers et al (AT2 of IDS filed on 11/12/2003, 1993, Urol. Res. 21:452, Abstract No.P42, Springer International).

Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 24, 25, 27, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Bussemakers et al (AT2 of IDS filed on 11/12/2003, 1993, Urol. Res. 21:452, Abstract No.P42, Springer International) as evidenced by Bussenmakers et al (Cancer Res. 1999 Dec 1;59(23):5975-9) and Figs. 3 of the instant specification.

Claims 1, 2, and 25 read on any nucleic acid longer than SEQ ID NO:2 (278 nucleotide) because the claims do not specify any structure of the claimed nucleic acid molecule(s) and does not specify any function of the claimed nucleic acid, either. Claim 3 also reads on any unidentified nucleic acid molecule because the claims are drawn to at least 90 % identical to a unknown sequence i.e., nucleotide sequence which

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hybridizes under high stringency conditions to 27 to 254 of SEQ ID NO:1 or the full complement thereof. Claims 4 and 5 are interpreted as any nucleic acid comprising instant SEQ ID NO:1. Claims 24, and 31 reads on any nucleic acid that comprises 27 to 254 of SEQ ID NO:1. Claim 27 reads on any nucleic acid with similarity to instant SEQ ID NO:1 due to the limitation in (c), "a nucleotide sequence which hybridizes under high stringency condition to any of the nucleotide sequence".

Bussemakers et al teach two isolated nucleic acid molecules longer than instant SEQ ID NO:2 i.e., 2.2 and 4.0 kb transcripts associated with prostate cancer. Bussemakers et al call DD3; instant claims 1, 2, 25 read on the 2.2 and 4.0 kb transcripts detected with DD3 probes of the art. It appears that the 2.2 and 4.0 kb transcripts is capable of hybridizing to a nucleic acid sequence comprising a polynucleotide sequence at least 90 % identical to 27 to 254 of SEQ ID NO:1 or its full complement (instant claim 3), and also hybridizes to the nucleic acid comprising instant SEQ ID NO:1 (instant claim 27) because instant SEQ ID NO:1 appears to be inserted into the 2.2 and/or 4 kb based on instant Figs 1-3. It appears that 2.2 and 4.0 kb transcripts of the Bussenmakers et al (1993) same transcript as the 2 and 4 kb transcripts shown at Fig. 3 of Bussenmakers et al (1999). Based on instant Fig. 1, it appears PCA3 and DD3 refer to a single entity.

Although instant claims 4, 5, 24, and 31 specifically recites the minimum structural requirement i.e., SEQ ID NO:1 or encodes instant SEQ ID NO:3, nucleotide 27-254 of SEQ ID NO:1 and the art does not specifically teach the specifically recited sequences, the claimed nucleotide molecules appear to be the same as the prior art

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because they appear to come from same human gene, DD3(PCA3), both are involved in prostate cancer development and detected in prostate cancers only. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the composition of the prior art does not possess the same material, structural and functional characteristics of the instantly claimed composition. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed composition is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

The **rejection** of claims 1-3, 5, 10-12 set forth in the Office action mailed 1/11/2002 is **reinstated**, and claims 4, 24-34 are also rejected under 35 U.S.C. 102(a) as being anticipated by WO 98/45420 (IDS AL1 filed on 03/19/2001, 10/15/1998).

Claims 1, 2, and 25 read on any nucleic acid longer than SEQ ID NO:2 (278 nucleotide) because the claims do not specify any structure of the claimed nucleic acid molecule(s) and does not specify any function of the claimed nucleic acid, either. Claim 3 also reads on any unidentified nucleic acid molecule because the claims are drawn to at least 90 % identical to a unknown sequence i.e., nucleotide sequence which hybridizes under high stringency conditions to 27 to 254 of SEQ ID NO:1 or the full complement thereof. Claims 4 and 5 are interpreted as any nucleic acid comprising instant SEQ ID NO:1. Claims 24, and 31 reads on any nucleic acid that comprises 27 to 254 of SEQ ID NO:1. Claim 27 reads on any nucleic acid with similarity to instant SEQ ID NO:1 due to the limitation in (c), "a nucleotide sequence which hybridizes under high

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stringency condition to any of the nucleotide sequence". The dependent claims 10-12, 28-30, 32-34 are drawn to a recombinant nucleic acid molecules made from the base claims, a cell or a non-human organism containing said recombinant nucleic acid molecules.

Applicant at page 8 of the amendment filed on 7/11/2002 argued that Bussemakers does not teach or suggest: (1) the long PCA3 sequence (SEQ ID NO:1) or the sequence spanning nucleotides 27-254 of SEQ ID NO:1; (2) that the short and long sequences of PCA3 can be linked to a cancer or normal phenotype, respectively; and (3) that the additional sequence of SEQ ID NO:1, interrupts the PCA3 open reading frame, thereby truncating PCA3 open reading (as set forth in SEQ ID NO:3). Thus, since Bussemakers does not teach the nucleotide sequence set forth from nucleotides 27 to 254 of SEQ ID NO:1, it cannot teach SEQ ID NO:4 which is an example of an oligonucleotide which specifically hybridizes to a subset of the sequence spanning from nucleotides 27 to 254 of SEQ ID NO:1. These arguments have been fully considered but found unpersuasive because instant claims 1-3, and 25 do not necessarily require instant SEQ ID NO:1, therefore it is concluded that applicant's argument is directed at a limitation not present in the claims. Claim 5 is interpreted as open because it depends on claim 1 which recites "having", therefore the claimed nucleic acid is not limited to nucleic acid encoding SEQ ID NO:3 but also encompasses the nucleic acid of the prior art which encode all of instant SEQ ID NO:3 plus some other amino acids.

Although instant claims 4, 5, 24, and 31 specifically recites the minimum structural requirement i.e., SEQ ID NO:1, nucleotide 27-254 of SEQ ID NO:1 and the art

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does not specifically teach the specifically recited sequences, the claimed nucleotide molecules appear to be the same as the prior art because they appear to come from same human gene, DD3(PCA3), both are involved in prostate cancer development and detected in prostate cancers only. It appears that instant SEQ ID NO:1 lies between exon 3 and 4a of the PCA3 transcription unit. Not the front page of the art. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the composition of the prior art does not possess the same material, structural and functional characteristics of the instantly claimed composition. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed composition is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Allowable Subject Matter

Claims 6, and 9 are allowed because claim 6 is interpreted as drawn to a primer consisting of 10 to 50 consecutive nucleotides of nucleotide 27 to 254 of SEQ ID NO:1 and claim 9 is interpreted as drawn to kit comprising said primer inside a container.

Conclusion

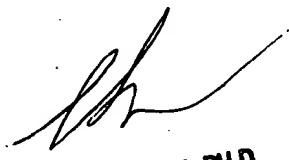
Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Misook Yu, Ph.D.
February 6, 2004.



LARRY E. HELMS, PH.D.
PRIMARY EXAMINER

7/11/2002

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BUSSE *et al.*
Appl. No. 09/675,650

37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Claims:

Please cancel claims 7-8 and 13-23 without prejudice to or disclaimer of the subject matter contained therein. Applicants reserve the right to prosecute the subject matter of these claims in one or more continuing or divisional applications.

Please substitute the following claim 1 for the pending claim 1:

B¹
1. (Once Amended) An isolated nucleic acid molecule encoding a differentially expressed prostate cancer antigen 3 (PCA3) mRNA containing an additional sequence between exon 3 and exon 4a, thereby giving rise to a PCA3 mRNA, having a sequence which is longer than that set forth in SEQ ID NO:2.

Please substitute the following claim 3 for the pending claim 3:

B²
3. (Once Amended) The isolated nucleic acid molecule according to claim 1, comprising a polynucleotide sequence at least 90% identical to a sequence selected from the group consisting of:

- (a) a nucleotide sequence as set forth from nucleotides 27 to 254 of SEQ ID NO:1;
- (b) a nucleotide sequence fully complementary to the nucleotide sequence in (a);